

|   |   |                                 |
|---|---|---------------------------------|
| <b>Form PTO-1427</b><br><b>U.S. Department of Commerce</b><br><b>Patent and Trademark Office</b><br><br><b>INFORMATION DISCLOSURE CITATION</b><br>(Use several sheets if necessary) | <b>Atty. Docket No.</b><br>2259/66844-B/<br>JPW/AJM/CY/SK | <b>Serial No.</b><br>10/687,396 |
|   | <b>Applicant(s)</b><br>A. Raymond Frackelton, Jr. et al.  |                                 |
|   | <b>Filing Date</b><br>October 15, 2003                    | <b>Group Art Unit</b><br>1647   |

### U.S. PATENT DOCUMENTS

| Examiner Initials | Document Number    | Date    | Name              | Class | Subclass | Filing Date If Appropriate |
|-------------------|--------------------|---------|-------------------|-------|----------|----------------------------|
|                   | 2004 0 0 3 3 5 4 2 | 2/19/04 | Frackelton et al. |       |          |                            |

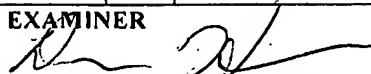
### FOREIGN PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Translation |    |
|-------------------|-----------------|------|------|-------|----------|-------------|----|
|                   |                 |      |      |       |          | Yes         | No |
|                   |                 |      |      |       |          |             |    |
|                   |                 |      |      |       |          |             |    |

### OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |  |
|----|--|
| DH | American Cancer Society, "Breast cancer facts & figures 2001-2002." <u>American Cancer Society Surveillance Research</u> . (2001);   |
| DH | Andrechek, E.R., et al., "Tyrosine kinase signaling in breast cancer: tyrosine kinase-mediated signal transduction in transgenic mouse models of human breast cancer." <u>Breast Cancer Res.</u> , 2(3):211-6. (2000); |
| DH | Batzer, A.G., et al., "Hierarchy of binding sites for Grb2 and Shc on the epidermal growth factor receptor." <u>Mol. Cell. Biol.</u> , 14(8):5192-201. (1994);   |
| DH | Baumann, C. A., et al., "CAP defines a second signaling pathway required for insulin-stimulated glucose transport." <u>Nature</u> , 407(6801):202-7. (2000);   |
| DH | Ben-Levy, R., et al., "A single autophosphorylation site confers oncogenicity to the Neu/ErbB-2 receptor and enables coupling to the MAP kinase pathway." <u>EMBO J.</u> , 13(14):3302-11. (1994);                     |
| DH | Berger, M.S., et al., "Correlation of c-erbB-2 gene amplification and protein expression in human breast carcinoma with nodal status and nuclear grading." <u>Cancer Research</u> , 48(5):1238-43. (1988);             |

EXAMINER



DATE CONSIDERED

3/13/06

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
2259/66844-B/  
JPW/AJM/CY/SKSerial No.  
10/687,396INFORMATION DISCLOSURE CITATION  
(Use several sheets if necessary)Applicant(s)  
A. Raymond Frackelton, Jr. et al.Filing Date  
October 15, 2003Group Art Unit  
1647

## U.S. PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Filing Date If Appropriate |
|-------------------|-----------------|------|------|-------|----------|----------------------------|
|                   |                 |      |      |       |          |                            |
|                   |                 |      |      |       |          |                            |

## FOREIGN PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Translation |    |
|-------------------|-----------------|------|------|-------|----------|-------------|----|
|                   |                 |      |      |       |          | Yes         | No |
|                   |                 |      |      |       |          |             |    |
|                   |                 |      |      |       |          |             |    |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |   |
|----|---|
| DH | Besson, A., et al., "PTEN/MMAC1/TEP1 in signal transduction and tumorigenesis." <u>Eur. J. Biochem.</u> , 263(3):605-11. (1999);  |
| DH | Boney, C.M., et al., "The critical role of Shc in insulin-like growth factor-I-mediated mitogenesis and differentiation in 3T3-L1 preadipocytes." <u>Mol. Endocrinol.</u> , 14(6):805-13. (2000);                                 |
| DH | Boylan, J.M., et al., "Uncoupling of hepatic, epidermal growth factor-mediated mitogen-activated protein kinase activation in the fetal rat." <u>J. Biol. Chem.</u> , 273(6):3784-90. (1998);                                     |
| DN | Brown, N.S., et al., "Hypoxia and oxidative stress in breast cancer. Oxidative stress: its effects on the growth, metastatic potential and response to therapy of breast cancer." <u>Breast Cancer Res.</u> , 3(5):323-7. (2001); |
| DH | Buday, L. et al., "Epidermal growth factor regulates p21ras through the formation of a complex of receptor, Grb2 adaptor protein, and Sos nucleotide exchange factor." <u>Cell</u> , 73(3):611-20. (1993);                        |
| DH | Buday, L., et al., "Downregulation of the Ras activation pathway by MAP kinase phosphorylation of Sos." <u>Oncogene</u> , 11(7):1327-31. (1995);  |

EXAMINER

DATE CONSIDERED

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

|   |   |                                   |
|---|---|-----------------------------------|
| <b>Form PTO-1449</b><br><br><b>U.S. Department of Commerce</b><br><b>Patent and Trademark Office</b><br><br><b>INFORMATION DISCLOSURE CITATION</b><br>(Use several sheets if necessary) | <b>Atty. Docket No.</b><br>2259/66844-B/<br>JPW/AJM/CY/SK | <b>Serial No.</b><br>10/687,396   |
|   | <b>Applicant(s)</b><br>A. Raymond Fräckelton, Jr. et al.  |                                   |
|   | <b>Filing Date</b><br>October 15, 2003                    | <b>Group Art Unit</b><br>1647/643 |

## U.S. PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Filing Date If Appropriate |
|-------------------|-----------------|------|------|-------|----------|----------------------------|
|                   |                 |      |      |       |          |                            |
|                   |                 |      |      |       |          |                            |

## FOREIGN PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Translation |    |
|-------------------|-----------------|------|------|-------|----------|-------------|----|
|                   |                 |      |      |       |          | Yes         | No |
|                   |                 |      |      |       |          |             |    |
|                   |                 |      |      |       |          |             |    |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |   |
|----|---|
| DH | Bundred, N.J., et al., "Studies of epidermal growth factor receptor inhibition in breast cancer." <u>Endocr. Relat. Cancer</u> 8(3):183-9. (2001);  |
| DH | Carraway, K.L., et al., "A new acquaintance for erbB3 and erbB4: a role for receptor heterodimerization in growth signaling." <u>Cell</u> , 78(1):5-8. (1994);  |
| DH | Carraway, K.L., et al., "Heregulin stimulates mitogenesis and phosphatidylinositol 3-kinase in mouse fibroblasts transfected with erbB2/neu and erbB3." <u>J. Biol. Chem.</u> , 270(13):7111-6. (1995);               |
| DH | Chen, D., et al., "SOS phosphorylation and disassociation of the Grb2-SOS complex by the ERK and JNK signaling pathways." <u>J. Biol. Chem.</u> , 271(11):6328-32. (1996);  |
| DH | Clark, J.W., et al., "Effects of tyrosine kinase inhibitors on the proliferation of human breast cancer cell lines and proteins important in the Ras signaling pathway." <u>Int. J. Cancer</u> , 65(2):186-91 (1996); |
| DH | Cohen, G.B., et al., "Modular binding domains in signal transduction proteins." <u>Cell</u> , 80(2):237-48 (1995);  |

|  |                                   |
|--|-----------------------------------|
| <b>EXAMINER</b><br> | <b>DATE CONSIDERED</b><br>3/13/06 |
|--|-----------------------------------|

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
2259/66844-B/  
JPW/AJM/CY/SKSerial No.  
10/687,396INFORMATION DISCLOSURE CITATION  
(Use several sheets if necessary)Applicant(s)  
A. Raymond Frackelton, Jr. et al.Filing Date  
October 15, 2003

Group Art Unit

1647  
1643

## U.S. PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Filing Date If Appropriate |
|-------------------|-----------------|------|------|-------|----------|----------------------------|
|                   |                 |      |      |       |          |                            |
|                   |                 |      |      |       |          |                            |

## FOREIGN PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Translation |    |
|-------------------|-----------------|------|------|-------|----------|-------------|----|
|                   |                 |      |      |       |          | Yes         | No |
|                   |                 |      |      |       |          |             |    |
|                   |                 |      |      |       |          |             |    |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |  |
|----|--|
| DH | Collins, L.R., et al., "Bifurcation of cell migratory ad proliferative signaling by adapter protein Shc." <u>J. Cell. Biol.</u> , 147(7):1561-8. (1999);   |
| DH | Culouscou, J.M., et al., "Characterization of a breast cancer cell differentiation factor that specifically activates the HER4/p180erbB4 receptor." <u>J. Biol. Chem.</u> , 268(25):18407-10. (1993);  |
| DH | Dankort D., et al., "Multiple erbb-2/Neu phosphorylation sites mediate transformation through distinct effector proteins." <u>J. Biol. Chem.</u> 276(42):38921-8. (2001);  |
| DH | Davol, P.A., et al., "Requirement for Shc phosphorylation in insulin-like growth factor-1 signaling to mitogen-activated protein kinase through the epidermal growth factor receptor in the prostrate adenocarcinoma cell line PC-3." <u>Proceedings AACR</u> , 42:5156. (2001); |
| DH | Dickson, C., et al., "Tyrosine kinase signaling in breast cancer: fibroblast growth factors and their receptors." <u>Breast Cancer Res.</u> , 2(3):191-6. (2000);  |
| DH | Dickson, R.B., et al., "Breast cancer: influence of endocrine hormones, growth factors and genetic alterations." <u>Adv. Exp. Med. Biol.</u> , 330:119-41. (1993);   |

EXAMINER

DATE CONSIDERED

3/13/06

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
2259/66844-B/  
JPW/AJM/CY/SKSerial No.  
10/687,396INFORMATION DISCLOSURE CITATION  
(Use several sheets if necessary)Applicant(s)  
A. Raymond Frackelton, Jr. et al.Filing Date  
October 15, 2003

Group Art Unit

1647  
1643

## U.S. PATENT DOCUMENTS

| Examiner<br>Initials | Document Number | Date | Name | Class | Subclass | Filing Date<br>If Appropriate |
|----------------------|-----------------|------|------|-------|----------|-------------------------------|
|                      |                 |      |      |       |          |                               |
|                      |                 |      |      |       |          |                               |

## FOREIGN PATENT DOCUMENTS

| Examiner<br>Initials | Document Number | Date | Name | Class | Subclass | Translation |    |
|----------------------|-----------------|------|------|-------|----------|-------------|----|
|                      |                 |      |      |       |          | Yes         | No |
|                      |                 |      |      |       |          |             |    |
|                      |                 |      |      |       |          |             |    |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |  |
|----|--|
| DH | Dickson, R.B., et al., "Growth factors in breast cancer." <u>Endocr. Rev.</u> , 16(5):559-89. (1995);  |
| DH | Dougall, W.C., et al., "The neu-oncogene: signal transduction pathways, transformation mechanisms and evolving therapies." <u>Oncogene</u> , 9(8):2109-23. (1994);   |
| DH | Ennis, B.W., et al., "Anti-epidermal growth factor receptor antibodies inhibit the autocrine- stimulated growth of MDA-468 human breast cancer cells." <u>Mol. Endocrinol.</u> , 3(11):1830-8. (1989);   |
| DH | Faisal, A., et al. "Serine/threonine phosphorylation of ShcA. Regulation of protein-tyrosine phosphatase-pest binding and involvement in insulin signaling." <u>J. Biol. Chem.</u> , 277(33): 30144-52. (2002);  |
| DH | Feig, L.A., "Guanine-nucleotide exchange factors: a family of positive regulators of Ras and related GTPases." <u>Curr. Opin. Cell. Biol.</u> , 6(2):204-11. (1994);   |
| DH | Filardo, E.J., et al., "Estrogen-induced activation of Erk-1 and Erk-2 requires the G protein-coupled receptor homolog, GPR30, and occurs via trans-activation of the epidermal growth factor receptor through release of HB-EGF." <u>Mol. Endocrinol.</u> , 14(10):1649-60. (2000); |

EXAMINER

DATE CONSIDERED

3/13/06

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
2259/66844-B/  
JPW/AJM/CY/SKSerial No.  
10/687,396INFORMATION DISCLOSURE CITATION  
(Use several sheets if necessary)Applicant(s)  
A. Raymond Frackelton, Jr. et al.Filing Date  
October 15, 2003

Group Art Unit

~~1647~~ 1643

## U.S. PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Filing Date If Appropriate |
|-------------------|-----------------|------|------|-------|----------|----------------------------|
|                   |                 |      |      |       |          |                            |
|                   |                 |      |      |       |          |                            |

## FOREIGN PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Translation |    |
|-------------------|-----------------|------|------|-------|----------|-------------|----|
|                   |                 |      |      |       |          | Yes         | No |
|                   |                 |      |      |       |          |             |    |
|                   |                 |      |      |       |          |             |    |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |   |
|----|---|
| DH | Goldhirsch, A., et al., "Meeting highlights: international consensus panel on the treatment of primary breast cancer. Seventh International Conference on Adjuvant Therapy of Primary Breast Cancer." <u>J. Clin. Oncol.</u> , 19(18):3817-27. (2001);                            |
| DH | Gotoh, N., et al., "The SH2 domain of Shc suppresses EGF-induced mitogenesis in a dominant negative manner." <u>Oncogene</u> , 11(12):2525-33. (1995);  |
| DH | Gotoh, N., et al., "A novel pathway from phosphorylation of tyrosine residues 239/240 of Shc, contributing to suppress apoptosis by IL-3." <u>EMBO. J.</u> , 15(22):6197-204. (1996);   |
| DH | Gotoh, N., et al., "Tyrosine phosphorylation sites at amino acids 239 and 240 of Shc are involved in epidermal growth factor-induced mitogenic signaling that is distinct from Ras/mitogen-activated protein kinase activation." <u>Mol. Cell. Biol.</u> , 17(4):1824-31. (1997); |
| DH | Gresham, J., et al., "Involvement of Shc in the signaling response of human prostrate tumor cell lines to epidermal growth factor." <u>Int. J. Cancer</u> , 77(6):923-7. (1998);  |
| DH | Gu, J., et al., "Shc and FAK differentially regulate cell motility and directionality modulated by PTEN." <u>J. Cell. Biol.</u> , 146(2):389-403. (1999);   |

EXAMINER

DATE CONSIDERED

3/13/06

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
2259/66844-B/  
JPW/AJM/CY/SKSerial No.  
10/687,396INFORMATION DISCLOSURE CITATION  
(Use several sheets if necessary)Applicant(s)  
A. Raymond Frackelton, Jr. et al.Filing Date  
October 15, 2003Group Art Unit  
1647/1643

## U.S. PATENT DOCUMENTS

| Examiner<br>Initials | Document Number | Date | Name | Class | Subclass | Filing Date<br>If Appropriate |
|----------------------|-----------------|------|------|-------|----------|-------------------------------|
|                      |                 |      |      |       |          |                               |
|                      |                 |      |      |       |          |                               |

## FOREIGN PATENT DOCUMENTS

| Examiner<br>Initials | Document Number | Date | Name | Class | Subclass | Translation |    |
|----------------------|-----------------|------|------|-------|----------|-------------|----|
|                      |                 |      |      |       |          | Yes         | No |
|                      |                 |      |      |       |          |             |    |
|                      |                 |      |      |       |          |             |    |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |  |
|----|--|
| DH | Gu, H., et al., "New role for Shc in activation of the phosphatidylinositol 3-kinase/Akt pathway." <u>Mol. Cell. Biol.</u> , 20(19):7109-20. (2000);   |
| DH | Hamilton, J.A., et al., "The expression profile for the tumor suppressor gene PTEN and associated polymorphic markers." <u>Br. J. Cancer</u> , 82(10):1671-6. (2000);                                    |
| DH | Hashimoto, A., et al., "Shc regulates epidermal growth factor-induced activation of the JNK signaling pathway." <u>J. Biol. Chem.</u> , 274(29):20139-43. (1999);  |
| DH | Hayes, D.F., et al., "Prognostic factors in breast cancer: current and new predictors of metastasis." <u>J. Mammary Gland Biol. Neoplasia</u> , 6(4):375-92. (2001);                                     |
| DH | Hines, S.J., et al., "Coexpression of the c-kit and stem cell factor genes in breast carcinomas." <u>Cell. Growth Differ.</u> , 6(6):769-79. (1995);   |
| DH | Hudziak, R., et al., "Increased expression of the putative growth factor receptor p185HER2 causes transformation and tumorigenesis of NIH3T3 cells." <u>Proc. Natl. Acad. Sci.</u> , 84:7159-63. (1987); |

EXAMINER

DATE CONSIDERED

3/13/06

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
2259/66844-B/  
JPW/AJM/CY/SKSerial No.  
10/687,396INFORMATION DISCLOSURE CITATION  
(Use several sheets if necessary)Applicant(s)  
A. Raymond Frackelton, Jr. et al.Filing Date  
October 15, 2003

Group Art Unit

1647  
1643

## U.S. PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Filing Date If Appropriate |
|-------------------|-----------------|------|------|-------|----------|----------------------------|
|                   |                 |      |      |       |          |                            |
|                   |                 |      |      |       |          |                            |

## FOREIGN PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Translation |    |
|-------------------|-----------------|------|------|-------|----------|-------------|----|
|                   |                 |      |      |       |          | Yes         | No |
|                   |                 |      |      |       |          |             |    |
|                   |                 |      |      |       |          |             |    |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |   |
|----|---|
| DM | Hynes, N., "Amplification and overexpression of the erbB-2 gene in human tumors: its involvement in tumor development, significance as a prognostic factor, and potential as a target for cancer therapy." <u>Seminars in Cancer Biology</u> , 4:19-26. (1993); |
| DH | Hynes, N.E. "Tyrosine kinase signaling in breast cancer." <u>Breast Cancer Res.</u> , 2(3):154-7. (2000);   |
| DH | Irani, K., et al., "Mitogenic signaling mediated by oxidants in Ras-transformed fibroblasts." <u>Science</u> , 275(5306):1649-52. (1997);   |
| DH | Janes, P.W., et al., "Activation of the Ras signalling pathway in human breast cancer cells overexpressing erbB-2." <u>Oncogene</u> , 9(12):3601-8. (1994);   |
| DH | Karin, M., et al., "Transcriptional control by protein phosphorylation: signal transmission from the cell surface to the nucleus." <u>Curr. Biol.</u> , 5(7):747-57. (1995);  |
| DH | Li, L., et al., "Single-cell MALDI: a new tool for direct peptide profiling." <u>Trends Biotechnol.</u> , 18(4):151-60. (2000);   |

EXAMINER

DATE CONSIDERED

3/13/06

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



|   |   |                                    |
|---|---|------------------------------------|
| <b>Form PTO-1449</b><br><br><b>U.S. Department of Commerce</b><br><b>Patent and Trademark Office</b><br><br><b>INFORMATION DISCLOSURE CITATION</b><br>(Use several sheets if necessary) | <b>Atty. Docket No.</b><br>2259/66844-B/<br>JPW/AJM/CY/SK | <b>Serial No.</b><br>10/687,396    |
|   | <b>Applicant(s)</b><br>A. Raymond Frackelton, Jr. et al.  |                                    |
|   | <b>Filing Date</b><br>October 15, 2003                    | <b>Group Art Unit</b><br>1647/1643 |

### U.S. PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Filing Date If Appropriate |
|-------------------|-----------------|------|------|-------|----------|----------------------------|
|                   |                 |      |      |       |          |                            |
|                   |                 |      |      |       |          |                            |

### FOREIGN PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Translation |    |
|-------------------|-----------------|------|------|-------|----------|-------------|----|
|                   |                 |      |      |       |          | Yes         | No |
|                   |                 |      |      |       |          |             |    |
|                   |                 |      |      |       |          |             |    |

### OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |  |
|----|--|
| DH | Luttrell, D.K., et al., "Involvement of pp60c-src with two major signaling pathways in human breast cancer." <u>Proc. Natl. Acad. Sci. USA</u> , 91(1):83-7. (1994);   |
| DH | Luttrell, L.M., et al., "G-protein-coupled receptors and their regulation: activation of the MAP kinase signaling pathway by G-protein-coupled receptors." <u>Adv. Second Messenger Phosphoprotein Res.</u> , 31:263-77. (1997); |
| DH | Matoskova, B., et al., "Constitutive phosphorylation of eps8 in tumor cell lines: relevance to malignant transformation." <u>Mol. Cell. Biol.</u> , 15(7):3805-12. (1995);   |
| DH | McGuire, W., et al., "How to use prognostic factors in auxiliary node-negative breast cancer patients." <u>J. Natl. Cancer Inst.</u> , 82:1006-12. (1990);   |
| DH | Meyer, S., et al., "Analysis of the role of the Shc and Grb2 proteins in signal transduction by the v-ErbB protein." <u>Mol. Cell. Biol.</u> , 14(5):3253-62. (1994);  |
| DH | Migliaccio, E., et al., "Opposite effects of the p52shc/p46shc and p66shc splicing isoforms on the EGF receptor-MAP kinase-fos signaling pathway." <u>EMBO. J.</u> , 16(4):706-16. (1997);                                       |

EXAMINER

DATE CONSIDERED



3/13/06

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
2259/66844-B/  
JPW/AJM/CY/SKSerial No.  
10/687,396INFORMATION DISCLOSURE CITATION  
(Use several sheets if necessary)Applicant(s)  
A. Raymond Frackelton, Jr. et al.Filing Date  
October 15, 2003Group Art Unit  
~~1647~~ 1643

## U.S. PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Filing Date If Appropriate |
|-------------------|-----------------|------|------|-------|----------|----------------------------|
|                   |                 |      |      |       |          |                            |
|                   |                 |      |      |       |          |                            |

## FOREIGN PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Translation |    |
|-------------------|-----------------|------|------|-------|----------|-------------|----|
|                   |                 |      |      |       |          | Yes         | No |
|                   |                 |      |      |       |          |             |    |
|                   |                 |      |      |       |          |             |    |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |   |
|----|---|
| DM | Migliaccio, E., et al., "The p66shc adaptor protein controls oxidative stress response and life span in mammals." <u>Nature</u> , 402(6759):309-13. (1999);   |
| DM | Mitchell, P.J., et al., "Cloning and characterization of cDNAs encoding a novel non-receptor tyrosine kinase, brk, expressed in human breast tumours." <u>Oncogene</u> , 9(8):2383-90. (1994);  |
| DM | Nemoto, S., et al., "Redox regulation of forkhead proteins through a p66shc-dependent signaling pathway." <u>Science</u> , 295(5564):2450-2. (2002);  |
| DM | Nguyen, D.H., et al. "Urokinase-type plasminogen activator stimulates the Ras/Extracellular signal-regulated kinase (ERK) signaling pathway and MCF-7 cell migration by a mechanism that requires focal adhesion kinase, Src, and Shc. Rapid dissociation of GRB2/Sps-Shc complex is associated with the transient phosphorylation of ERK in urokinase-treated cells." <u>J. Biol. Chem.</u> 275(25):19382-8. (2000); |
| DM | Nolan, M.K., et al., "Differential roles of IRS-1 and SHC signaling pathways in breast cancer cells." <u>Int. J. Cancer</u> , 72(5):828-34. (1997);   |
| DM | Normanno, N., et al., "Amphiregulin as an autocrine growth factor for c-Ha-ras- and c-erbB-2- transformed human mammary epithelial cells." <u>Proc. Natl. Acad. Sci. USA</u> , 91(7):2790-4. (1994);  |

EXAMINER

DATE CONSIDERED

3/13/06

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

|   |  |  |  |  |  |                             |  |
|---|--|--|--|--|--|-----------------------------|--|
| Form PTO-1449   |  | U.S. Department of Commerce<br>Patent and Trademark Office |  | Atty. Docket No.<br>2259/66844-B/<br>JPW/AJM/CY/SK |  | Serial No.<br>10/687,396    |  |
| <b>INFORMATION DISCLOSURE CITATION</b><br>(Use several sheets if necessary) |  |  |  | Applicant(s)<br>A. Raymond Frackelton, Jr. et al.  |  |                             |  |
|   |  |  |  | Filing Date<br>October 15, 2003                    |  | Group Art Unit<br>1647 1643 |  |

| U.S. PATENT DOCUMENTS |  |                 |      |      |       |          |                            |
|-----------------------|--|-----------------|------|------|-------|----------|----------------------------|
| Examiner Initials     |  | Document Number | Date | Name | Class | Subclass | Filing Date If Appropriate |
|                       |  |                 |      |      |       |          |                            |
|                       |  |                 |      |      |       |          |                            |
|                       |  |                 |      |      |       |          |                            |

| FOREIGN PATENT DOCUMENTS |  |                 |      |      |       |          |             |    |
|--------------------------|--|-----------------|------|------|-------|----------|-------------|----|
| Examiner Initials        |  | Document Number | Date | Name | Class | Subclass | Translation |    |
|                          |  |                 |      |      |       |          | Yes         | No |
|                          |  |                 |      |      |       |          |             |    |
|                          |  |                 |      |      |       |          |             |    |
|                          |  |                 |      |      |       |          |             |    |

| OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) |   |
|--|---|
| DH   | Okada, S., et al., "The 66-kDa Shc isoform is a negative regulator of the epidermal growth factor-stimulated mitogen-activated protein kinase pathway." <u>J. Biol. Chem.</u> , 272(44):28042-9. (1997);  |
| DH   | Panchamoorthy, G., et al. "p120cbl is a major substrate of tyrosine phosphorylation upon B cell antigen receptor stimulation and interacts in vivo with Fyn and Syk tyrosine kinases, Grb2 and Shc adaptors, and the p85 subunit of phosphatidylinositol 3-kinase." <u>J. Biol. Chem.</u> 271(6):3187-94. (1996); |
| DH   | Pawson, T., et al., "Signal transduction and growth control in normal and cancer cells." <u>Curr. Opin. Genet. Dev.</u> , 4(1):1-4. (1994);   |
| DH   | Pawson, T., "Protein modules and signaling networks." <u>Nature</u> , 373(6515):573-80. (1995 65);  |
| DH   | Pellicci, G., et al., "A novel transforming protein (SHC) with an SH2 domain is implicated in mitogenic signal transduction." <u>Cell</u> , 70(1):93-104. (1992);   |
| DH   | Pellicci, G., et al., "The mitogenic and mitogenic responses to HGF are amplified by the Shc adaptor protein." <u>Oncogene</u> , 10(8):1631-8. (1995);  |

|              |                            |
|--------------|----------------------------|
| EXAMINER<br> | DATE CONSIDERED<br>3/13/06 |
|--------------|----------------------------|

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
2259/66844-B/  
JPW/AJM/CY/SKSerial No.  
10/687,396**INFORMATION DISCLOSURE CITATION**  
(Use several sheets if necessary)Applicant(s)  
A. Raymond Frackelton, Jr. et al.Filing Date  
October 15, 2003Group Art Unit  
1647

1643

**U.S. PATENT DOCUMENTS**

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Filing Date If Appropriate |
|-------------------|-----------------|------|------|-------|----------|----------------------------|
|                   |                 |      |      |       |          |                            |
|                   |                 |      |      |       |          |                            |

**FOREIGN PATENT DOCUMENTS**

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Translation |    |
|-------------------|-----------------|------|------|-------|----------|-------------|----|
|                   |                 |      |      |       |          | Yes         | No |
|                   |                 |      |      |       |          |             |    |
|                   |                 |      |      |       |          |             |    |

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

|    |  |
|----|--|
| DH | Pietrzkowski, Z., et al., "Inhibition of growth of prostatic cancer cell lines by peptide analogues of insulin-like growth factor." <u>Cancer Res.</u> , 53(5):1102-6. (1993);   |
| DH | Ravichandran, K.S. "Signaling via Shc family adapter proteins." <u>Oncogene</u> , 20(44):6322-30. (2001);  |
| DH | Rozakis-Adcock, M., et al., "Association of the Shc and Grb2/Sem5 SH2-containing proteins is implicated in activation of the Ras pathway by tyrosine kinases." <u>Nature</u> , 360(6405):689-92. (1992);                     |
| DH | Sasaoka, T., et al., "Evidence for a functional role of Shc proteins in mitogenic signaling induced by insulin, insulin-like growth factor-I, and epidermal growth factor." <u>J. Biol. Chem.</u> , 269(18):13689-94 (1994); |
| DH | Schechter, A.L., et al., "The neu oncogene: an erb-B-related gene encoding a 185,000-Mr tumour antigen." <u>Nature</u> , 312(5994):513-6. (1984);  |
| DH | Scita, G., et al., "EPS8 and E3B1 transduce signals from Ras to Rac." <u>Nature</u> , 401(6750):290-3. (1999);   |

EXAMINER

*Dr. R*

DATE CONSIDERED

3/13/06

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
2259/66844-B/  
JPW/AJM/CY/SKSerial No.  
10/687,396INFORMATION DISCLOSURE CITATION  
(Use several sheets if necessary)Applicant(s)  
A. Raymond Frackelton, Jr. et al.Filing Date  
October 15, 2003Group Art Unit  
~~1647~~ 1643

## U.S. PATENT DOCUMENTS

| Examiner<br>Initials | Document Number | Date | Name | Class | Subclass | Filing Date<br>If Appropriate |
|----------------------|-----------------|------|------|-------|----------|-------------------------------|
|                      |                 |      |      |       |          |                               |
|                      |                 |      |      |       |          |                               |

## FOREIGN PATENT DOCUMENTS

| Examiner<br>Initials | Document Number | Date | Name | Class | Subclass | Translation |    |
|----------------------|-----------------|------|------|-------|----------|-------------|----|
|                      |                 |      |      |       |          | Yes         | No |
|                      |                 |      |      |       |          |             |    |
|                      |                 |      |      |       |          |             |    |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |  |
|----|--|
| DH | Segatto, O., et al., "Shc products are substrates of erbB-2 kinase." <u>Oncogene</u> , 8(8):2105-12. (1993);   |
| DH | Seger, R., et al., "The MAPK signaling cascade." <u>FASEB. J.</u> , 9(9):726-35. (1995);   |
| DH | Sepp-Lorenzino, L., et al., "Signal transduction pathways induced by heregulin in MDA-MB-453 breast cancer cells." <u>Oncogene</u> , 12(8):1679-87. (1996);  |
| DH | Singh, A., et al., "Insulin-like growth factor type I and insulin-like growth factor type II stimulate oestradiol-17 beta hydroxysteroid dehydrogenase (reductive) activity in breast cancer cells." <u>J. Endocrinol</u> 129(2):R5-8. (1991); |
| DH | Slamon, D.J., et al., "Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene." <u>Science</u> , 235:177-82. (1987);  |
| DH | Songyang, Z., et al., "SH2 domains recognize specific phosphopeptide sequences." <u>Cell</u> , 72(5):767-78. (1993);   |

EXAMINER

DATE CONSIDERED

3/13/06

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation: not in conformance and not considered. Include copy of this form with next communication to applicant.

|   |  |  |  |
|---|--|--|--|
| Form PTO-1449   | U.S. Department of Commerce<br>Patent and Trademark Office | Atty. Docket No.<br>2259/66844-B/<br>JPW/AJM/CY/SK | Serial No.<br>10/687,396               |
| <b>INFORMATION DISCLOSURE CITATION</b><br>(Use several sheets if necessary) |  | Applicant(s)<br>A. Raymond Frackelton, Jr. et al.  |  |
|   |  | Filing Date<br>October 15, 2003                    | Group Art Unit<br><del>1647</del> 1643 |

**U.S. PATENT DOCUMENTS**

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Filing Date If Appropriate |
|-------------------|-----------------|------|------|-------|----------|----------------------------|
|                   |                 |      |      |       |          |                            |
|                   |                 |      |      |       |          |                            |
|                   |                 |      |      |       |          |                            |

**FOREIGN PATENT DOCUMENTS**

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Translation |    |
|-------------------|-----------------|------|------|-------|----------|-------------|----|
|                   |                 |      |      |       |          | Yes         | No |
|                   |                 |      |      |       |          |             |    |
|                   |                 |      |      |       |          |             |    |
|                   |                 |      |      |       |          |             |    |

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

|    |   |
|----|---|
| DH | Stern, D.F., "Tyrosine kinase signaling in breast cancer: ErbB family receptor tyrosine kinases." <u>Breast Cancer Res.</u> , 2(3):176-83. (2000);  |
| DH | Stevenson, L.E., et al., "Constitutively tyrosine phosphorylated p52 Shc in breast cancer cells: Correlation with ErbB2 and p66 Shc expression." <u>Breast Cancer Res. Treat.</u> , 49(2):119-28. (1998);       |
| DH | Stevenson, L.E., et al., "Shc dominant negative disrupts cell cycle progression in both G0/G1 and G2/M of ErbB2 positive breast cancer cells." <u>Cell. Growth &amp; Differentiation</u> , 10(1):61-71. (1999); |
| DH | Sutherland, R.L., et al., "Cyclin gene expression and growth control in normal and neoplastic human breast epithelium." <u>J. Steroid Biochem. Mol. Biol.</u> , 47(1-6):99-106. (1993);                         |
| DH | Trusolino, L., et al., "A signaling adapter function for alpha6beta4 integrin in the control of HGF-dependent invasive growth." <u>Cell</u> , 107(5):643-54 (2001);   |
| DH | Tuck, A.B., et al., "Coexpression of hepatocyte growth factor and receptor (Met) in human breast carcinoma." <u>Am. J. Pathol.</u> , 148(1):225-32. (1996);   |

EXAMINER

DATE CONSIDERED



3/13/06

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

|   |   |                                    |
|---|---|------------------------------------|
| <b>Form PTO-1449</b><br><br><b>U.S. Department of Commerce</b><br><b>Patent and Trademark Office</b><br><br><b>INFORMATION DISCLOSURE CITATION</b><br>(Use several sheets if necessary) | <b>Atty. Docket No.</b><br>2259/66844-B/<br>JPW/AJM/CY/SK | <b>Serial No.</b><br>10/687,396    |
|   | <b>Applicant(s)</b><br>A. Raymond Frackelton, Jr. et al.  |                                    |
|   | <b>Filing Date</b><br>October 15, 2003                    | <b>Group Art Unit</b><br>1647 1643 |

### U.S. PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Filing Date If Appropriate |
|-------------------|-----------------|------|------|-------|----------|----------------------------|
|                   |                 |      |      |       |          |                            |
|                   |                 |      |      |       |          |                            |

### FOREIGN PATENT DOCUMENTS

| Examiner Initials | Document Number | Date | Name | Class | Subclass | Translation |    |
|-------------------|-----------------|------|------|-------|----------|-------------|----|
|                   |                 |      |      |       |          | Yes         | No |
|                   |                 |      |      |       |          |             |    |
|                   |                 |      |      |       |          |             |    |

### OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |   |
|----|---|
| DH | Ventura, A., et al., "The p66Shc longevity gene is silenced through epigenetic modifications of an alternative promoter." <u>J. Biol. Chem.</u> , 277(25):22370-6. (2002);  |
| DH | Webster, M.A., et al., "Requirement for both Shc and phosphatidylinositol 3' kinase signaling pathways in polyomavirus middle T-mediated mammary tumorigenesis." <u>Mol. Cell. Biol.</u> , 18(4):2344-59. (1998);                     |
| DH | Whittal, R.M., et al., "Nanoliter chemistry combined with mass spectrometry for peptide mapping of proteins from single mammalian cell lysates." <u>Anal. Chem.</u> , 70(24):5344-7. (1998);  |
| DH | Xie, Y., et al., "Tyrosine phosphorylation of Shc proteins and formation of Shc/Grb2 complex correlate to the transformation of NIH3T3 cells mediated by the point-mutation activated neu." <u>Oncogene</u> , 10(12):2409-13. (1995); |
| DH | Yarden, Y., "Biology of HER 2 and its importance in breast cancer." <u>Oncology</u> , 61 (Suppl 2):1-13. (2001);  |
| DH | Zhang, X., et al. Tyrosine kinase signaling in breast cancer: insulin-like growth factors and their receptors in breast cancer." <u>Breast Cancer Res</u> , 2(3):170-5. (2000); and   |
| DH | Zhao, H., et al., "Insulin receptor-mediated dissociation of Grb2 from Sos involves phosphorylation of Sos by kinase(s) other than extracellular signal-regulated kinase." <u>J. Biol. Chem.</u> , 273(20):12061-7. (1998).           |

EXAMINER

DATE CONSIDERED



3/13/06

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

PTO-1449 REPRODUCED

ATTORNEY DOCKET NO.  
3887.1000-001APPLICATION NO.  
10/687,396INFORMATION DISCLOSURE STATEMENT  
IN AN APPLICATIONFIRST NAMED INVENTOR  
A. Raymond Frackelton, Jr.FILING DATE  
October 15, 2003

February 23, 2006

EXAMINER  
Humphrey, David HaroldCONFIRMATION NO.  
2101GROUP  
1643

(Use several sheets if necessary)

## U.S. PATENT DOCUMENTS

| EXAM-<br>INER<br>INITIAL | REF.<br>NO. | DOCUMENT NUMBER<br>Number-Kind Code (if known) | ISSUE DATE /<br>PUBLICATION DATE<br>MM-DD-YYYY | NAME OF PATENTEE OR APPLICANT<br>OF CITED DOCUMENT |
|--------------------------|-------------|--|--|--|
| DH                       | A1          | 2004/0209809 A1                                | 10-21-2004                                     | Saucier, <i>et al.</i>                             |
| DH                       | A2          | 5,912,183                                      | 06-15-1999                                     | Comoglio, <i>et al.</i>                            |
| DH                       | A3          | 6,492,138 B1                                   | 12-10-2002                                     | McGlade, <i>et al.</i>                             |
| DH                       | A4          | 6,025,145 A                                    | 02-15-2000                                     | Godowski, <i>et al.</i>                            |
| DH                       | A5          | 6,777,415 A                                    | 08-17-2004                                     | Daley, <i>et al.</i>                               |

## FOREIGN PATENT DOCUMENTS

|  |    | DOCUMENT NUMBER<br>Country Code-Number-Kind Code<br>(if known) | DATE<br>MM-DD-YYYY | NAME OF PATENTEE OR APPLICANT<br>OF CITED DOCUMENT | TRANSLATION<br>YES NO |  |
|--|----|--|--------------------|--|-----------------------|--|
|  | B1 |  |                    |  |                       |  |
|  | B2 |  |                    |  |                       |  |
|  | B3 |  |                    |  |                       |  |
|  | B4 |  |                    |  |                       |  |
|  | B5 |  |                    |  |                       |  |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |    |   |
|----|----|---|
| DH | C1 | Bonati, A., <i>et al.</i> , "Selective Expression and Constitutive Phosphorylation of SHC Proteins in the CD34+ Fraction of Chronic Myelogenous Leukemias," <i>Cancer Research</i> 68:728-732 (2000).         |
| DH | C2 | Crowe, <i>et al.</i> , "Phosphorylation of the SHC Proteins on Tyrosine Correlates with the Transformation of Fibroblasts and Erythoroblasts by the v-Sea Tyrosine Kinase," <i>Oncogene</i> 9:537-544 (1994). |
| DH | C3 | McGlade, J., <i>et al.</i> , "Shc Proteins are Phosphorylated and Regulated by the v-Src and v-Fps Protein Tyrosine Kinases," <i>Proc. Natl. Acad. Sci.</i> 89:8869-8873 (1992).                              |
| DH | C4 | Pellicci, G., <i>et al.</i> , "Constitutive Phosphorylation of Shc Proteins in Human Tumors," <i>Oncogene</i> 11:899-907 (1995).  |
| DH | C5 | Yang, J., <i>et al.</i> , "Tyrosine Phosphorylation of Shc Proteins in Normal CD34+ Progenitor Cells and Leukemic Cells," <i>Blood</i> 94:373-374 (1999).   |

EXAMINER

DATE CONSIDERED

3/13/06